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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/471,749	12/23/99	HILLMAN J	PF-0519-1DIV

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EXAMINER	
HARRIS,A	
ART UNIT	**PAPER NUMBER**
1642	8

DATE MAILED: 06/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/471,749	Applicant(s) Hillman et al.
	Examiner Alana M. Harris, Ph. D.	Group Art Unit 1642

☒ Responsive to communication(s) filed on *May 8, 2000.*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *3, 6, 7, 9-12, and 19-40* is/are pending in the applicat

Of the above, claim(s) *3, 6, 7, 9-12, 19, 20, 23-26, and 29-40* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *21, 22, 27, and 28* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892 ✓

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2 and 5,* Filed March 10, 2000 & May 8, 2000, respectively.

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group I (newly added claims 21, 22, 27 and 28) in Paper No.4 (filed May 8, 2000) is acknowledged. The traversal is on the ground(s) that the search of Groups I-VII would substantially overlap between the groups and would not pose an undue burden on the Examiner. This is not found persuasive. The argument that Groups I-VII significantly overlap is not found persuasive because the claims of each Group are classified differently, necessitating different searches in the U.S. Patent shoes. Classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Further, Groups VI-VIII involve various method steps, which require additional searching.

The requirement is still deemed proper and is therefore made FINAL.

However, the policies set forth in the Commissioner's Notice of February 28, 1996 published on March 26, 1996 at 1184 O.G. 86 will be followed. Method claims limited to the scope of the allowable product claims will be rejoined and examined at the time the product claims are indicated as being allowable.

2. Claims 1, 2, 4, 5, 8 and 13-18 have been canceled.

Claims 21-40 have been added.

Claims 3, 6, 7, 9-12 and 19-40 are pending.

Claims 3, 6, 7, 9-12, 19-20, 23-26 and 29-40, drawn to non-elected inventions are withdrawn from examination.

Claims 21, 22, 27 and 28 are examined on the merits.

Priority

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

4. This application filed under former 37 CFR 1.62 lacks the necessary reference to the prior application. A statement reading "This is a divisional application of Application No. 09/078,402, filed May 13, 1998." should be entered following the title of the invention or as the first sentence of the specification.

5. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. § 120. U.S. Application Serial No. 09/078,402 filed May 13, 1998 from which priority is claimed was unavailable to the Examiner for review. Hence, claims 21, 22, 27 and 28 will not be granted the

May 13, 1998 priority date. Priority of the claims will be granted the effective filing date of the instant Application No. 09/471,749, filed on December 23, 1999.

Information Disclosure Statement

6. Applicant notified the Office in the Information Disclosure Citation (Paper No. 2, filed March 10, 2000) that listed documents to be considered were originally filed in parent case #09/078,402, filed May 13, 1998. Parent case #09/078,402 was unavailable to the Examiner, thus all documents "lined through" were not reviewed during examination. Applicant is invited to provide replacement copies of listed references for consideration.

Drawings

7. The drawings are objected to because of reasons cited on attached form, PTO948 completed by the draftsman. Correction is required.

Claim Rejections - 35 U.S.C. § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 21, 22, 27 and 28 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a. Claim 21b is broadly drawn to "a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO:3 or SEQ ID NO:5" and both 21c and d are drawn to "a biologically-active fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5, and an immunogenic fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5". The specification while being enabling for the polypeptides having the amino acid sequences of SEQ ID NO:3 or SEQ ID NO:5, does not reasonably provide enablement for variants that have at least 90% sequence identity. There is no guidance as to how to make these divergent sequences, which possess function with the absence of any information on what functions the native protein possesses. Likewise, it would seem that specific function(s) would be required to make a protein useful for the applications disclosed in the specification. The specification does not teach what those are or how to determine what they are. This could possibly be a vast collection of polypeptides and the specification provides inadequate instruction to allow one skilled in the art to make and use the said naturally occurring polypeptides having at least 90% sequence identity with a reasonable expectation of success and without undue experimentation.

b. Claims 27 and 28 are broadly drawn to "a pharmaceutical composition comprising an effective amount of polypeptide" and "a pharmaceutical composition...", respectively. The specification while being enabling for a composition comprising a polypeptide of claim 21 and a pharmaceutically acceptable carrier, does not reasonably provide enablement for a "pharmaceutical composition" comprising these same components. Claims drawn to "pharmaceutical compositions" are broadly interpreted to read on compositions effective for use as *in vivo* human therapeutics. The polypeptide of the invention is completely uncharacterized functionally. The mere fact that it seems to be expressed in various libraries (from cancerous tissue, reproductive tissues and gastrointestinal tissue) is not sufficient to establish that it plays a role in the pathology or etiology of diseases in these tissues. In the absence of an established role of the polypeptide in diseases of the aforementioned tissues it is impossible to predict what if any therapeutic effect the administration of the polypeptide would have for the treatment of cancer. The selection and development of such human therapeutics is art known to be highly unpredictable. The specification exemplifies no examples of the effective use of the effective use of the polypeptide as a pharmacological agent and no such uses are art known. One skilled in the art would not know how to use the claimed compositions as the component polypeptide was not known prior to the applicant's invention. Its function is not known and is not disclosed in the specification, which speculates merely that it is "associated" with apoptosis. The "associated" protein claimed is not known to be useful for the treatment of disorders with increased or decreased apoptosis. Such disorders can include, but are not limited to, atherosclerosis and

cancers such as leukemia, systemic lupus erythematosus and Chrohn's disease. Therefore, due to the unpredictability of therapeutics and the absence of any evidence concerning the effectiveness of the claimed pharmaceutical composition as a pharmacological agent, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use with a reasonable expectation of success, the invention commensurate in scope with this claim. The association provides no guidance as to how the instant polypeptides can be employed as therapeutic nor a basis to predict their efficacy. The applicant is advised to amend the claim to delete the recitation of "pharmaceutical".

c. Claim 27 is broadly drawn to "...an effective amount...". The claimed invention is not described in such, full clear and concise exact terms to enable any person skilled in the art to make and use the same. The claim fails to state the function which is to be achieved by an "effective amount" and the specification provides no such guidance. One of skill in the art would not have a reasonable expectation of success in practicing the claimed invention and one skilled in the art would not be able to practice the claimed invention without undue experimentation.

10. Claims 21 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 21 is broadly drawn to a purified polypeptide comprising an amino sequence selected from a biologically-active fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5 and an immunogenic fragment of the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5. This claim is drawn to a polypeptide fragment that contains a small number of amino acid residues that is less than the 238 amino acids of SEQ ID NO:3 and 410 amino acids of SEQ ID NO:5, hence the claim is drawn to amino acid residues that minimally contain only portions of SEQ ID NO:3 and 5. Thus, the claims are drawn to a large genus of molecules. In the case of small identified amino acid residues claimed with open language, the genus of polypeptides comprising only a partial sequence encompasses a variety of subgenera with widely varying attributes. The specification discloses only the structural features of one species, the polypeptide sequence of SEQ ID NO:3 and SEQ ID NO:5. The specification lacks information to lead one of skill in the art to understand that the applicant had possession of the broadly claimed invention at the time the instant application was filed. Applicant is referred to the interim guidelines concerning compliance with the written description requirement of 35 U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 21, 22, 27 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitations "naturally-occurring", 'biologically-active" and "immunogenic" in claim 21 are not clear. What functional properties are bestowed upon these designated sequences described by these terms?

b. The phrase "effective amount" in claim 27 is vague and indefinite when the claims fail to state the function which is to be achieved.

Claim Rejections - 35 U.S.C. § 101

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 21, 22, 27 and 28 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The applicant has asserted several utilities for the claimed purified polypeptide and fragments. The specification asserts the following utilities for the claimed polypeptide, as well as fragments of the sequence: compositions for the diagnosis, prevention or treatment of disorders associated with increased or decreased apoptosis. However, these asserted utilities are not

credible, specific or substantial for the broadly claimed polypeptide. Other that the sequence identification number, the specification provides no functional characterization of the polypeptide, no specific tissue distribution of the polypeptide and no specific disease state in which these proteins affect. The broadly claimed polypeptides belong to a group, collectively referred to as human apoptosis associated proteins (HAPOP). The group encompasses individual proteins: "HAPOP-1", "HAPOP-2", "HAPOP-3" and "HAPOP-4". This protein according to the specification, page 8, lines 16-19 can be obtained from any species (i.e. bovine, equine or human) and from any source whether natural, synthetic or recombinant. This protein is also expressed in a wide variety of cells and tissues as indicated in northern analysis. HAPOP polypeptides have been suggested to prevent or treat cell proliferative disorders such as sarcoma, cancers of the cervix, ganglia, testis and a host of other disorders affecting immunocompromised individuals. Consequently, there is no information that links expression of the claimed polypeptide to **any specific** tissue or disorder. Thus, the asserted utility of the claimed nucleic acids is not substantial, specific or credible.

Claims 21, 22, 27 and 28 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 U.S.C. § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

16. Claims 21 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,925,733 (filed June 11, 1996). Sequence 32 of U.S. Patent # 5,925,733 (see column 119) discloses a substantially purified polypeptide comprising an amino acid sequence that is a fragment of the amino acid sequence of SEQ ID NO:3. In the instant case, amino acid residues # 179-183 correspond with amino acids # 44-48 of SEQ. ID. NO:3, which would be biologically-active and an immunogenic and is the same as that claimed. Also disclosed is a pharmaceutical composition comprising an effective amount of a polypeptide of claim 21 and a pharmaceutically acceptable excipient (claim 27), see column 47, lines 41-65.

17. Claims 21 and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent #5,919,660 (filed June 24, 1997). Sequence 2 of U.S. Patent # 5,919,660 (see column 41) discloses a substantially purified polypeptide comprising an amino acid sequence that is a fragment

of the amino acid sequence of SEQ ID NO:5. In the instant case, amino acid residues # 315-320 correspond with amino acids # 319-324 of SEQ ID NO:5, which would be biologically-active and an immunogenic and is the same as that claimed. Also disclosed is a pharmaceutical composition comprising an effective amount of a polypeptide of claim 21 and a pharmaceutically acceptable excipient (claim 27), see bridging paragraph of columns 29 and 30, lines 41-65.

18. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated Accession # A42445 (March 3, 1993). Accession # A42445 discloses a substantially purified polypeptide comprising an amino acid sequence that is a fragment of the amino acid sequence of SEQ ID NO:3. For example in the instant case, amino acids # 137-165 of attached amino acid database sheet corresponds with amino acids # 137-165 of SEQ ID NO:3, which would be biologically-active and immunogenic and is the same as that claimed.

19. Claim 21 is rejected under 35 U.S.C. 102(b) as being anticipated Accession # A55302 (July 8, 1995) or Gabig et al. (J. Biol. Chem. 269:29515-29519, 1994). Accession # A55302 or Gabig et al. disclose a substantially purified polypeptide comprising an amino acid sequence that is a fragment of the amino acid sequence of SEQ ID NO:5. For example in the instant case, amino acids # 281-287 of attached amino acid database sheet corresponds with amino acids # 319-325 of SEQ ID NO:5, which would be biologically-active and immunogenic and is the same as that claimed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris whose telephone number is (703)306-5880. The examiner can normally be reached on Monday through Friday from 6:30 am to 3:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703)308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703)308-0196.

Alana M. Harris, Ph.D.
Patent Examiner, Group 1642
June 19, 2000

NANCY A. JOHNSON, PH.D
PRIMARY EXAMINER